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STRUCTURE FILE UPDATES:   12 JUL 2009  HIGHEST RN 1161919-42-1
DICTIONARY FILE UPDATES:  12 JUL 2009  HIGHEST RN 1161919-42-1

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http://www.cas.org/support/stngen/stndoc/properties.html

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L1           1 CEDIRANIB/CN

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L1   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2009 ACS on STN
RN   288383-20-0  REGISTRY
ED   Entered STN:  08 Sep 2000
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CN Quinazoline, 4-[(4-fluoro-2-methyl-1H-indol-5-yl)oxy]-6-methoxy-7-[3-(1-pyrrolidinyl)propoxy]- (CA INDEX NAME)
OTHER NAMES:
CN 4-(4-Fluoro-2-methylindol-5-yloxy)-6-methoxy-7-[3-(pyrrolidin-1-yl)propoxy]quinazoline
CN AZD 2171
CN Cediranib
CN ZD 2171
DR 790713-41-6, 557795-03-6
MF C25 H27 F N4 O3
CI COM
SR CA
LC STN Files: ADISINSIGHT, CA, CAPLUS, CASREACT, CHEMCATS, CSCHEM, EMBASE, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, IPA, PROUSDDR, RTECS*, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
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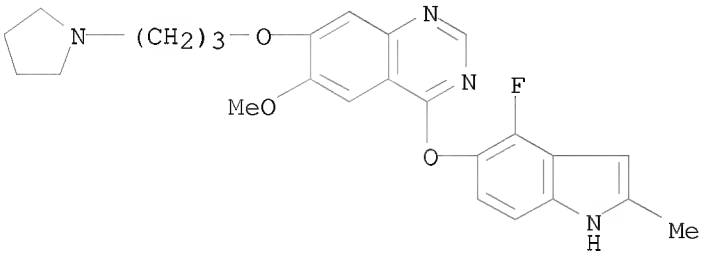

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

87 REFERENCES IN FILE CA (1907 TO DATE)
5 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
87 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> fil caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	7.88	8.10

FILE 'CAPLUS' ENTERED AT 13:30:39 ON 13 JUL 2009

FILE COVERS 1907 - 13 Jul 2009 VOL 151 ISS 3
FILE LAST UPDATED: 12 Jul 2009 (20090712/ED)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Apr 2009

USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Apr 2009

CAplus now includes complete International Patent Classification (IPC) reclassification data for the second quarter of 2009.

CAS Information Use Policies apply and are available at:

http://www.cas.org/legal/infopolicy.html

This file contains CAS Registry Numbers for easy and accurate substance identification.

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=> l1
L2          87 L1

=> l2 and py<2005
      25140894 PY<2005
L3            5 L2 AND PY<2005

=> d l3 ibib abs 1-5

L3   ANSWER 1 OF 5  CAPLUS  COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER:         2004:995977  CAPLUS
DOCUMENT NUMBER:          141:420417
TITLE:                    Therapeutic agents comprising an anti-angiogenic agent
                          in combination with an Src inhibitor for use in
                          normotensive treatment of angiogenesis
INVENTOR(S):              Curwen, Jon Owen; Wedge, Stephen Robert
PATENT ASSIGNEE(S):       Astrazeneca AB, Swed.; Astrazeneca UK Limited
SOURCE:                   PCT Int. Appl., 111 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
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     WO 2004098604         A1    20041118    WO 2004-GB1939          20040504 <--
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             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
             NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
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     AU 2004237132         B2    20071018
     CA 2519930            A1    20041118    CA 2004-2519930         20040504 <--
     EP 1620104            A1    20060201    EP 2004-731049          20040504
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     BR 2004009742         A     20060509    BR 2004-9742            20040504
     CN 1784232            A     20060607    CN 2004-80012089        20040504
     CN 100418531          C     20080917
     JP 2006525304         T     20061109    JP 2006-506222          20040504
     NZ 542348             A     20090131    NZ 2004-542348          20040504
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NO 2005004411	A	20051130	NO 2005-4411		20050923
ZA 2005008858	A	20070328	ZA 2005-8858		20051101
US 20060223815	A1	20061005	US 2005-555389		20051103
MX 2005011858	A	20060217	MX 2005-11858		20051104
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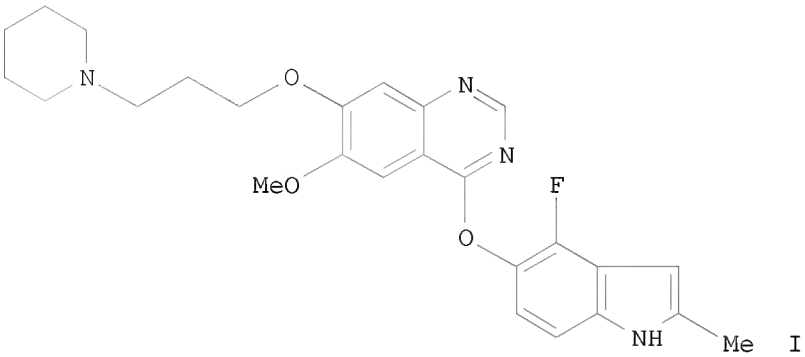

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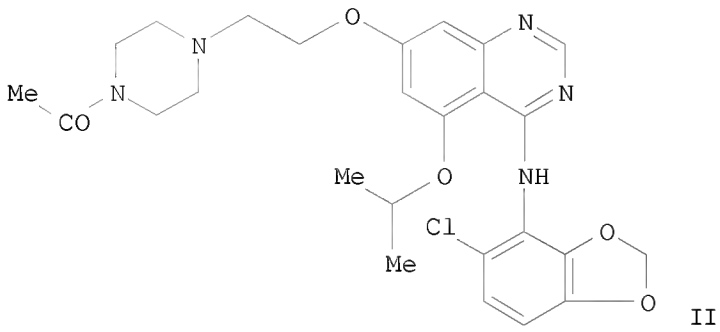

II

AB The invention relates to the use of an anti-angiogenic agent, such as I (preparation given), in combination with an inhibitor of the Src family of non-receptor tyrosine kinases, such as the II (prepns. according to a previous patent given), in the manufacture of a medicament for use in the substantially normotensive treatment in a warm-blooded mammal such as a human being of a disease state associated with angiogenesis. The invention provides for the Src kinase inhibitor to be administered in an amount effective to counteract substantially the hypertension induced by the anti-angiogenic agent. Thus, 7-(2-chloroethoxy)-4-(6-chloro-2,3-methylenedioxyanilino)-5-isopropoxyquinazoline was coupled with 1-acetylpiperazine using KI in DMA to give I. The diastolic blood pressure profile of rats over a 24 h period after administration of a combination of 1.5 mg/kg of I and 25 mg/kg of II demonstrated that the contrasting blood pressure effects of the antiangiogenic agent and the Src kinase inhibitor were substantially counterbalanced.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:965067 CAPLUS
DOCUMENT NUMBER: 141:406039
TITLE: Combinations for the treatment of diseases involving

cell proliferation, migration or apoptosis of myeloma cells, or angiogenesis

INVENTOR(S): Hilberg, Frank; Solca, Flavio; Stefanic, Martin Friedrich; Baum, Anke; Munzert, Gerd; Van Meel, Jacobus C. A.

PATENT ASSIGNEE(S): Boehringer Ingelheim International G.m.b.H., Germany; Boehringer Ingelheim Pharma G.m.b.H. & Co. K.-G.

SOURCE: PCT Int. Appl., 101 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004096224	A2	20041111	WO 2004-EP4363	20040424 <--
WO 2004096224	A3	20041216		
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RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1473043	A1	20041103	EP 2003-9587	20030429 <--
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CA 2523868	A1	20041111	CA 2004-2523868	20040424 <--
EP 1622619	A2	20060208	EP 2004-729366	20040424
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BR 2004009919	A	20060425	BR 2004-9919	20040424
JP 2006524634	T	20061102	JP 2006-500099	20040424
MX 2005011656	A	20051215	MX 2005-11656	20051028
NO 2005005605	A	20051128	NO 2005-5605	20051128

PRIORITY APPLN. INFO.:			
EP 2003-9587	A	20030429
EP 2004-508	A	20040113
EP 2004-1171	A	20040121
WO 2004-EP4363	W	20040424

AB The present invention relates to a pharmaceutical combination for the treatment of diseases which involves cell proliferation, migration or apoptosis of myeloma cells, or angiogenesis. The invention also relates to a method for the treatment of said diseases, comprising co-administration of effective amts. of specific active compds. and/or co-treatment with radiation therapy, in a ratio which provides an additive and synergistic effect, and to the combined use of these specific compds. and/or radiotherapy for the manufacture of corresponding pharmaceutical combination prepns. The pharmaceutical combination can include selected protein tyrosine kinase receptor antagonists and further chemotherapeutic or naturally occurring semisynthetic or synthetic agents.

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2003:532545 CAPLUS

DOCUMENT NUMBER: 139:95455
TITLE: Combined therapy against tumors comprising substituted acryloyl distamycin derivatives and protein kinase (serine/threonine kinase) inhibitors
INVENTOR(S): Geroni, Maria Cristina; Fowst, Camilla; Cozzi, Paolo
PATENT ASSIGNEE(S): Pharmacia Italia SpA, Italy
SOURCE: PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
WO 2003055522	A1	20030710	WO 2002-EP13092	20021218	<--
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CA 2472008	A1	20030710	CA 2002-2472008	20021218	<--
AU 2002352090	A1	20030715	AU 2002-352090	20021218	<--
AU 2002352090	B2	20080515			
EP 1461083	A1	20040929	EP 2002-787763	20021218	<--
EP 1461083	B1	20060329			
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BR 2002015454	A	20041123	BR 2002-15454	20021218	<--
HU 2004002639	A2	20050428	HU 2004-2639	20021218	
CN 1617744	A	20050518	CN 2002-827674	20021218	
JP 2005516025	T	20050602	JP 2003-556098	20021218	
AT 321572	T	20060415	AT 2002-787763	20021218	
ES 2263835	T3	20061216	ES 2002-787763	20021218	
NZ 533854	A	20070531	NZ 2002-533854	20021218	
RU 2328306	C2	20080710	RU 2004-123641	20021218	
MX 2004006543	A	20041004	MX 2004-6543	20040702	<--
ZA 2004005290	A	20050617	ZA 2004-5290	20040702	
IN 2004DN01960	A	20090403	IN 2004-DN1960	20040708	
NO 2004003217	A	20040730	NO 2004-3217	20040729	<--
US 20060084612	A1	20060420	US 2005-500606	20050505	
IN 2007DN00991	A	20070803	IN 2007-DN991	20070206	
PRIORITY APPLN. INFO.:			EP 2002-75052	A 20020102	
			WO 2002-EP13092	W 20021218	
			IN 2004-DN1960	A3 20040708	

OTHER SOURCE(S): MARPAT 139:95455
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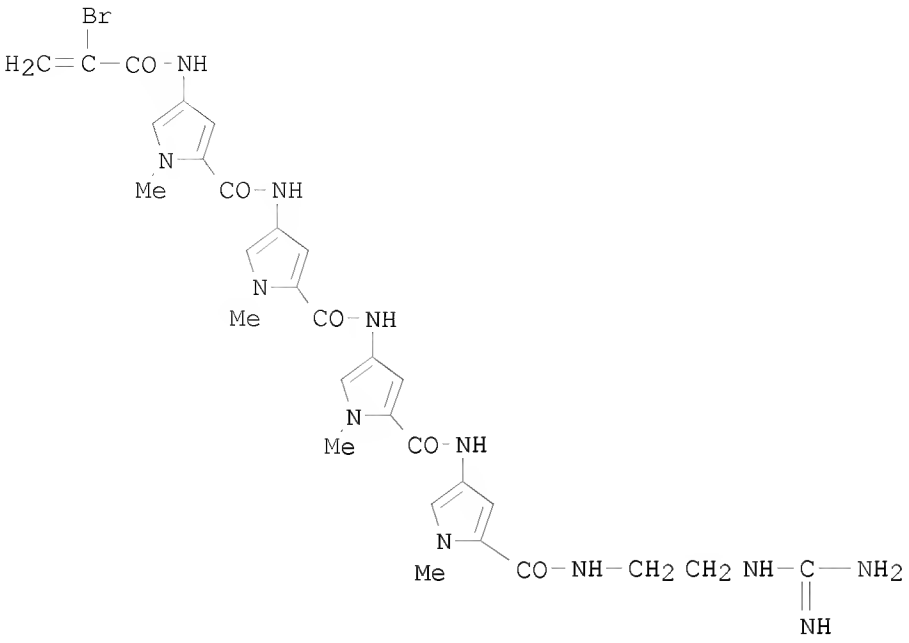

AB The present invention provides the combined use of acryloyl distamycin derivs., in particular α-bromo- and α-chloro-acryloyl distamycin derivs., and a protein kinase (serine/threonine and tyrosine kinases) inhibitor, in the treatment of tumors. Also provided is the use of the said combinations in the treatment or prevention of metastasis or in the treatment of tumors by inhibition of angiogenesis. An example protein kinase inhibitor is STI 571 and a distamycin derivative is brostallicin (I).

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2001:747609 CAPLUS
DOCUMENT NUMBER: 135:283196
TITLE: Therapeutic combinations of antihypertensive and antiangiogenic agents
INVENTOR(S): Curwen, Jon Owen; Ogilvie, Donald James
PATENT ASSIGNEE(S): Astrazeneca Ab, Swed.; Astrazeneca Uk Limited
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001074360	A1	20011011	WO 2001-GB1522	20010402 <--

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EP 1272186	A1	20030108	EP 2001-917305	20010402 <--
EP 1272186	B1	20070228		

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HU 2003000426	A2	20030628	HU 2003-426	20010402 <--
JP 2003528917	T	20030930	JP 2001-572104	20010402 <--
EE 200200578	A	20040615	EE 2002-578	20010402 <--
AU 2001244386	B2	20050127	AU 2001-244386	20010402
NZ 520938	A	20050826	NZ 2001-520938	20010402
AT 355065	T	20060315	AT 2001-917305	20010402
EP 1658849	A2	20060524	EP 2006-3576	20010402
EP 1658849	A3	20090218		

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NZ 534455	A	20070126	NZ 2001-534455	20010402
EP 1790340	A2	20070530	EP 2007-3863	20010402
EP 1790340	A3	20090318		

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ES 2280349	T3	20070916	ES 2001-917305	20010402
CZ 299410	B6	20080716	CZ 2002-3304	20010402
IN 2002MN01149	A	20050304	IN 2002-MN1149	20020823
ZA 2002006959	A	20031201	ZA 2002-6959	20020829 <--
US 20030144298	A1	20030731	US 2002-240413	20021001 <--
KR 849149	B1	20080731	KR 2002-713170	20021002
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NO 2002004814	A	20021112	NO 2002-4814	20021004 <--
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NO 2006002050	A	20011008	NO 2006-2050	20060508 <--
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PRIORITY APPLN. INFO.:	GB 2000-8269	A	20000405
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	NZ 2001-520938	A1	20010402
	WO 2001-GB1522	W	20010402
	KR 2002-713170	A3	20021002

OTHER SOURCE(S): MARPAT 135:283196

AB The invention concerns the use of a combination of an anti-angiogenic agent and an anti-hypertensive agent for use in the manufacture of a medicament for the treatment of a disease state associated with angiogenesis in a warm-blooded mammal, such as a human being. The invention also relates to pharmaceutical compns. comprising an anti-angiogenic agent and an anti-hypertensive agent, to kits thereof and to a method of treatment of a disease state associated with angiogenesis which comprises the administration of an effective amount of a combination of an anti-angiogenic agent and an anti-hypertensive agent to a warm-blooded animal, such as a human being. Anesthetized rats were dosed orally with 12.5 mg/kg of 4-(4-bromo-2-fluoroanilino)-6-methoxy-7-(1-methylpiperidin-4-ylmethoxy)quinazoline for 10 days, then they were dosed orally with 30 mg/kg captopril in addition to quinazoline compound The increase in diastolic blood pressure was reversed by the addition of captopril.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2000:573671 CAPLUS

DOCUMENT NUMBER: 133:177183

TITLE: Preparation of quinazoline derivatives as angiogenesis

inhibitors

INVENTOR(S): Hennequin, Laurent Francois Andre; Ple, Patrick; Stokes, Elaine Sophie Elizabeth; Mckerrecher, Darren

PATENT ASSIGNEE(S): Astrazeneca UK Limited, UK; Zeneca-Pharma S.A.

SOURCE: PCT Int. Appl., 346 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000047212	A1	20000817	WO 2000-GB373	20000208 <--
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JP 3893026	B2	20070314		
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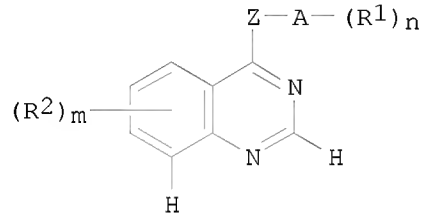
AU 763618	B2	20030731	AU 2000-24475	20000208 <--
NZ 513204	A	20040430	NZ 2000-513204	20000208 <--
CN 1167422	C	20040922	CN 2000-806085	20000208 <--
CN 1597667	A	20050323	CN 2004-10058982	20000208
CN 100360505	C	20080109		
TR 200500745	T2	20050523	TR 2005-745	20000208
NZ 530832	A	20050527	NZ 2000-530832	20000208
EP 1553097	A1	20050713	EP 2005-4285	20000208
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
AT 298237	T	20050715	AT 2000-902730	20000208
RU 2262935	C2	20051027	RU 2001-124816	20000208
ES 2242596	T3	20051116	ES 2000-902730	20000208
IL 144745	A	20081103	IL 2000-144745	20000208
EP 2050744	A1	20090422	EP 2008-168638	20000208
R: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE, AL, LT, LV, MK, RO, SI				
IN 2000DE00115	A	20050311	IN 2000-DE115	20000211
IN 2001MN00893	A	20070525	IN 2001-MN893	20010726
ZA 2001006340	A	20021101	ZA 2001-6340	20010801 <--
NO 2001003882	A	20011009	NO 2001-3882	20010809 <--
NO 321604	B1	20060612		
MX 2001008182	A	20030820	MX 2001-8182	20010810 <--
KR 838617	B1	20080616	KR 2001-710133	20010810
HK 1041212	A1	20051202	HK 2002-102781	20020412
US 7074800	B1	20060711	US 2002-913020	20020506
NO 2005002773	A	20011009	NO 2005-2773	20050608 <--

US 20060004017	A1	20060105	US 2005-169122		20050629
HK 1076104	A1	20081031	HK 2005-108262		20050921
JP 2006273860	A	20061012	JP 2006-129249		20060508
KR 2008015482	A	20080219	KR 2007-731001		20071231
PRIORITY APPLN. INFO.:			EP 1999-400305	A	19990210
			EP 2000-902730	A3	20000208
			EP 2005-4285	A3	20000208
			JP 2000-598164	A3	20000208
			WO 2000-GB373	W	20000208
			KR 2001-710133	A3	20010810
			US 2002-913020	A3	20020506

OTHER SOURCE(S): MARPAT 133:177183
GI



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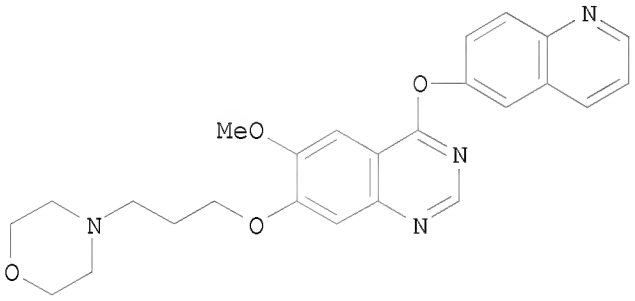


II

AB The title compds. (I) [wherein A = an 8-, 9-, 10-, 12- or 13-membered bicyclic or tricyclic ring optionally containing 1-3 O, N, and/or S heteroatoms; Z = O, NH, S, CH2, or a bond; n = 0-5; m = 0-3; R2 = H, OH, halo, CN, NO2, CF3, alkyl(sulfanyl), alkoxy, NR3N4, or R5X1; R3 and R4 = independently H or alkyl; X1 = a bond, O, CH2, OC(O), CO, S, SO, SO2, NR6CO, CONR7, SO2R8, NR9SO2, or NR10; R5 = H or (un)substituted alkyl, alkenyl, alkynyl, or heterocyclyl, etc.; R6-R10 = independently H or (alkoxy)alkyl] were prepared for use in the production of an antiangiogenic and/or vascular permeability reducing effect in warm-blooded animals. For instance, II was synthesized in a 9-step sequence starting with the cyclization of 2-amino-4-benzyloxy-5-methoxybenzamide using Gold's reagent in dioxane to form 7-benzyloxy-6-methoxy-3,4-dihydroquinazolin-4-one (84%). I and the pharmaceutically acceptable salts thereof inhibit the effects of VEGF, a property of value in the treatment of a number of disease states including cancer and rheumatoid arthritis (no data).

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d l3 ibib abs 1-5 hitstr

L3 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:995977 CAPLUS
DOCUMENT NUMBER: 141:420417

TITLE: Therapeutic agents comprising an anti-angiogenic agent in combination with an Src inhibitor for use in normotensive treatment of angiogenesis

INVENTOR(S): Curwen, Jon Owen; Wedge, Stephen Robert

PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited

SOURCE: PCT Int. Appl., 111 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

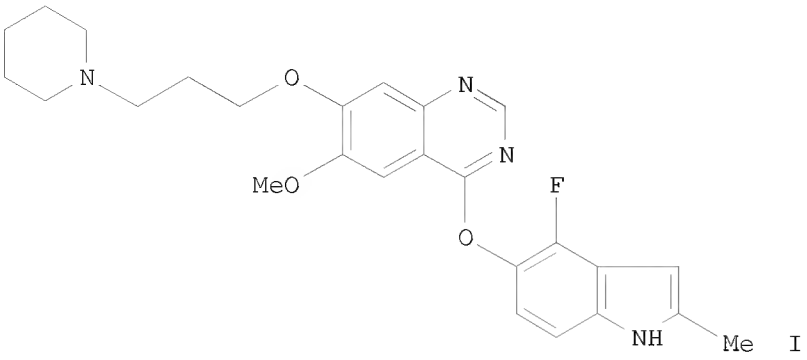
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004098604	A1	20041118	WO 2004-GB1939	20040504 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004237132	A1	20041118	AU 2004-237132	20040504 <--
AU 2004237132	B2	20071018		
CA 2519930	A1	20041118	CA 2004-2519930	20040504 <--
EP 1620104	A1	20060201	EP 2004-731049	20040504
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, HR				
BR 2004009742	A	20060509	BR 2004-9742	20040504
CN 1784232	A	20060607	CN 2004-80012089	20040504
CN 100418531	C	20080917		
JP 2006525304	T	20061109	JP 2006-506222	20040504
NZ 542348	A	20090131	NZ 2004-542348	20040504
NO 2005004411	A	20051130	NO 2005-4411	20050923
ZA 2005008858	A	20070328	ZA 2005-8858	20051101
US 20060223815	A1	20061005	US 2005-555389	20051103
MX 2005011858	A	20060217	MX 2005-11858	20051104
PRIORITY APPLN. INFO.:			GB 2003-10401 A	20030507
			WO 2004-GB1939 W	20040504

GI



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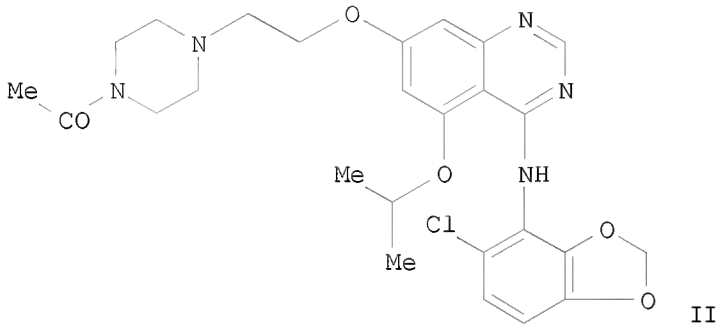


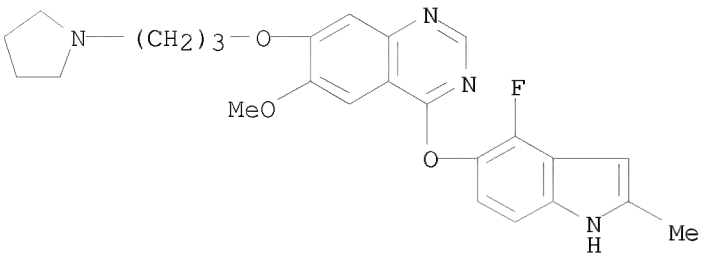
II

AB The invention relates to the use of an anti-angiogenic agent, such as I (preparation given), in combination with an inhibitor of the Src family of non-receptor tyrosine kinases, such as the II (prepns. according to a previous patent given), in the manufacture of a medicament for use in the substantially normotensive treatment in a warm-blooded mammal such as a human being of a disease state associated with angiogenesis. The invention provides for the Src kinase inhibitor to be administered in an amount effective to counteract substantially the hypertension induced by the anti-angiogenic agent. Thus, 7-(2-chloroethoxy)-4-(6-chloro-2,3-methylenedioxyanilino)-5-isopropoxyquinazoline was coupled with 1-acetylpiperazine using KI in DMA to give I. The diastolic blood pressure profile of rats over a 24 h period after administration of a combination of 1.5 mg/kg of I and 25 mg/kg of II demonstrated that the contrasting blood pressure effects of the antiangiogenic agent and the Src kinase inhibitor were substantially counterbalanced.

IT 288383-20-0, 4-(4-Fluoro-2-methylindol-5-yloxy)-6-methoxy-7-[3-(pyrrolidin-1-yl)propoxy]quinazoline
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(angiogenesis inhibitor; therapeutic agents comprising an anti-angiogenic agent in combination with an Src inhibitor for use in normotensive treatment of angiogenesis)

RN 288383-20-0 CAPLUS

CN Quinazoline, 4-[(4-fluoro-2-methyl-1H-indol-5-yl)oxy]-6-methoxy-7-[3-(1-pyrrolidinyl)propoxy]- (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:965067 CAPLUS
DOCUMENT NUMBER: 141:406039
TITLE: Combinations for the treatment of diseases involving cell proliferation, migration or apoptosis of myeloma cells, or angiogenesis
INVENTOR(S): Hilberg, Frank; Solca, Flavio; Stefanic, Martin Friedrich; Baum, Anke; Munzert, Gerd; Van Meel, Jacobus C. A.
PATENT ASSIGNEE(S): Boehringer Ingelheim International G.m.b.H., Germany; Boehringer Ingelheim Pharma G.m.b.H. & Co. K.-G.
SOURCE: PCT Int. Appl., 101 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004096224	A2	20041111	WO 2004-EP4363	20040424 <--
WO 2004096224	A3	20041216		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1473043	A1	20041103	EP 2003-9587	20030429 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AU 2004233576	A1	20041111	AU 2004-233576	20040424 <--
CA 2523868	A1	20041111	CA 2004-2523868	20040424 <--
EP 1622619	A2	20060208	EP 2004-729366	20040424
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
BR 2004009919	A	20060425	BR 2004-9919	20040424
JP 2006524634	T	20061102	JP 2006-500099	20040424
MX 2005011656	A	20051215	MX 2005-11656	20051028
NO 2005005605	A	20051128	NO 2005-5605	20051128
PRIORITY APPLN. INFO.:			EP 2003-9587 A	20030429
			EP 2004-508 A	20040113

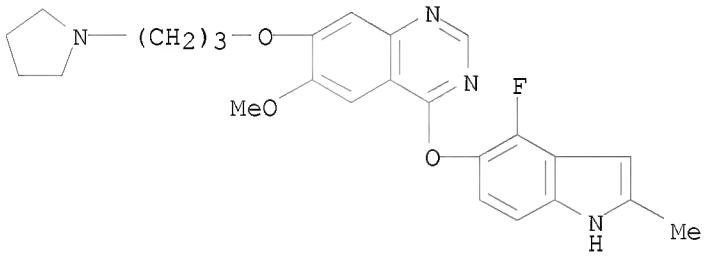
EP 2004-1171 A 20040121
WO 2004-EP4363 W 20040424

AB The present invention relates to a pharmaceutical combination for the treatment of diseases which involves cell proliferation, migration or apoptosis of myeloma cells, or angiogenesis. The invention also relates to a method for the treatment of said diseases, comprising co-administration of effective amts. of specific active compds. and/or co-treatment with radiation therapy, in a ratio which provides an additive and synergistic effect, and to the combined use of these specific compds. and/or radiotherapy for the manufacture of corresponding pharmaceutical combination prepns. The pharmaceutical combination can include selected protein tyrosine kinase receptor antagonists and further chemotherapeutic or naturally occurring semisynthetic or synthetic agents.

IT 288383-20-0
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug combinations for diseases involving cell proliferation and migration or apoptosis or angiogenesis including protein tyrosine kinase receptor antagonists and radiotherapy)

RN 288383-20-0 CAPLUS

CN Quinazoline, 4-[(4-fluoro-2-methyl-1H-indol-5-yl)oxy]-6-methoxy-7-[3-(1-pyrrolidinyl)propoxy]- (CA INDEX NAME)



REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2003:532545 CAPLUS
DOCUMENT NUMBER: 139:95455
TITLE: Combined therapy against tumors comprising substituted acryloyl distamycin derivatives and protein kinase (serine/threonine kinase) inhibitors
INVENTOR(S): Geroni, Maria Cristina; Fowst, Camilla; Cozzi, Paolo
PATENT ASSIGNEE(S): Pharmacia Italia SpA, Italy
SOURCE: PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003055522	A1	20030710	WO 2002-EP13092	20021218 <--

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UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2472008	A1	20030710	CA 2002-2472008	20021218	<--
AU 2002352090	A1	20030715	AU 2002-352090	20021218	<--
AU 2002352090	B2	20080515			
EP 1461083	A1	20040929	EP 2002-787763	20021218	<--
EP 1461083	B1	20060329			
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BR 2002015454	A	20041123	BR 2002-15454	20021218	<--
HU 2004002639	A2	20050428	HU 2004-2639	20021218	
CN 1617744	A	20050518	CN 2002-827674	20021218	
JP 2005516025	T	20050602	JP 2003-556098	20021218	
AT 321572	T	20060415	AT 2002-787763	20021218	
ES 2263835	T3	20061216	ES 2002-787763	20021218	
NZ 533854	A	20070531	NZ 2002-533854	20021218	
RU 2328306	C2	20080710	RU 2004-123641	20021218	
MX 2004006543	A	20041004	MX 2004-6543	20040702	<--
ZA 2004005290	A	20050617	ZA 2004-5290	20040702	
IN 2004DN01960	A	20090403	IN 2004-DN1960	20040708	
NO 2004003217	A	20040730	NO 2004-3217	20040729	<--
US 20060084612	A1	20060420	US 2005-500606	20050505	
IN 2007DN00991	A	20070803	IN 2007-DN991	20070206	

PRIORITY APPLN. INFO.: EP 2002-75052 A 20020102
WO 2002-EP13092 W 20021218
IN 2004-DN1960 A3 20040708

OTHER SOURCE(S): MARPAT 139:95455

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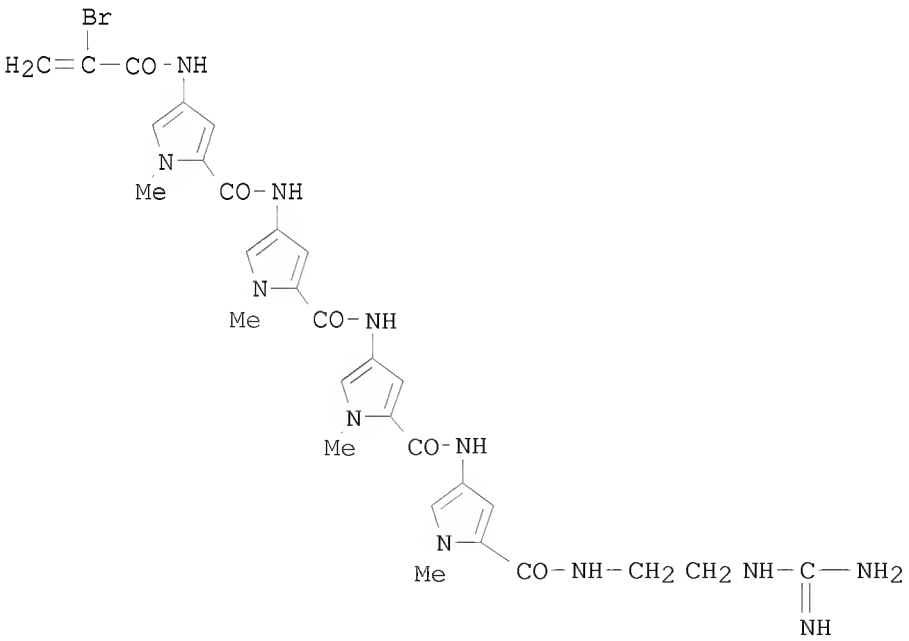


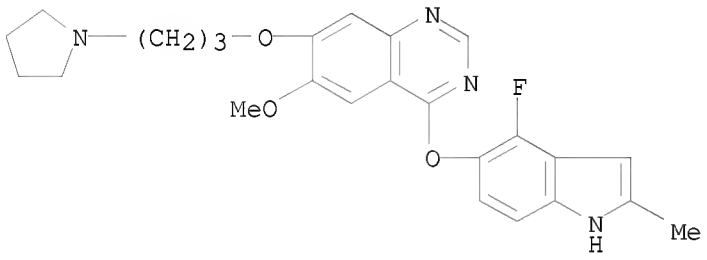
AB The present invention provides the combined use of acryloyl distamycin

derivs., in particular α-bromo- and α-chloro-acryloyl distamycin derivs., and a protein kinase (serine/threonine and tyrosine kinases) inhibitor, in the treatment of tumors. Also provided is the use of the said combinations in the treatment or prevention of metastasis or in the treatment of tumors by inhibition of angiogenesis. An example protein kinase inhibitor is STI 571 and a distamycin derivative is brostallicin (I).

IT 288383-20-0, ZD 2171
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combined antitumor therapy comprising acryloyl distamycin derivs. and protein kinase (serine/threonine kinase) inhibitors)

RN 288383-20-0 CAPLUS

CN Quinazoline, 4-[(4-fluoro-2-methyl-1H-indol-5-yl)oxy]-6-methoxy-7-[3-(1-pyrrolidinyl)propoxy]- (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2001:747609 CAPLUS
DOCUMENT NUMBER: 135:283196
TITLE: Therapeutic combinations of antihypertensive and antiangiogenic agents
INVENTOR(S): Curwen, Jon Owen; Ogilvie, Donald James
PATENT ASSIGNEE(S): Astrazeneca Ab, Swed.; Astrazeneca Uk Limited
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001074360	A1	20011011	WO 2001-GB1522	20010402 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2401854	A1	20011011	CA 2001-2401854	20010402 <--
EP 1272186	A1	20030108	EP 2001-917305	20010402 <--
EP 1272186	B1	20070228		
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BR 2001009729	A	20030204	BR 2001-9729	20010402	<--
HU 2003000426	A2	20030628	HU 2003-426	20010402	<--
JP 2003528917	T	20030930	JP 2001-572104	20010402	<--
EE 200200578	A	20040615	EE 2002-578	20010402	<--
AU 2001244386	B2	20050127	AU 2001-244386	20010402	
NZ 520938	A	20050826	NZ 2001-520938	20010402	
AT 355065	T	20060315	AT 2001-917305	20010402	
EP 1658849	A2	20060524	EP 2006-3576	20010402	
EP 1658849	A3	20090218			
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NZ 534455	A	20070126	NZ 2001-534455	20010402	
EP 1790340	A2	20070530	EP 2007-3863	20010402	
EP 1790340	A3	20090318			
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ES 2280349	T3	20070916	ES 2001-917305	20010402	
CZ 299410	B6	20080716	CZ 2002-3304	20010402	
IN 2002MN01149	A	20050304	IN 2002-MN1149	20020823	
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US 20030144298	A1	20030731	US 2002-240413	20021001	<--
KR 849149	B1	20080731	KR 2002-713170	20021002	
MX 2002009743	A	20030327	MX 2002-9743	20021003	<--
NO 2002004814	A	20021112	NO 2002-4814	20021004	<--
NO 323467	B1	20070521			
NO 2006002050	A	20011008	NO 2006-2050	20060508	<--
NO 326277	B1	20081027			
KR 2008034523	A	20080421	KR 2008-707835	20080331	

PRIORITY APPLN. INFO.:	GB 2000-8269	A	20000405
	EP 2001-917305	A3	20010402
	NZ 2001-520938	A1	20010402
	WO 2001-GB1522	W	20010402
	KR 2002-713170	A3	20021002

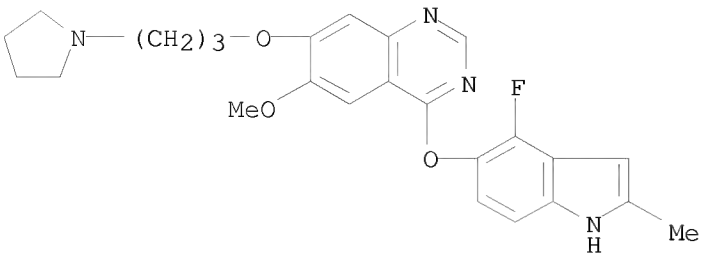
OTHER SOURCE(S): MARPAT 135:283196

AB The invention concerns the use of a combination of an anti-angiogenic agent and an anti-hypertensive agent for use in the manufacture of a medicament for the treatment of a disease state associated with angiogenesis in a warm-blooded mammal, such as a human being. The invention also relates to pharmaceutical compns. comprising an anti-angiogenic agent and an anti-hypertensive agent, to kits thereof and to a method of treatment of a disease state associated with angiogenesis which comprises the administration of an effective amount of a combination of an anti-angiogenic agent and an anti-hypertensive agent to a warm-blooded animal, such as a human being. Anesthetized rats were dosed orally with 12.5 mg/kg of 4-(4-bromo-2-fluoroanilino)-6-methoxy-7-(1-methylpiperidin-4-ylmethoxy)quinazoline for 10 days, then they were dosed orally with 30 mg/kg captopril in addition to quinazoline compound The increase in diastolic blood pressure was reversed by the addition of captopril.

IT 288383-20-0
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(therapeutic combinations of antihypertensive and antiangiogenic agents)

RN 288383-20-0 CAPLUS

CN Quinazoline, 4-[(4-fluoro-2-methyl-1H-indol-5-yl)oxy]-6-methoxy-7-[3-(1-pyrrolidinyl)propoxy]- (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2000:573671 CAPLUS
DOCUMENT NUMBER: 133:177183
TITLE: Preparation of quinazoline derivatives as angiogenesis inhibitors
INVENTOR(S): Hennequin, Laurent Francois Andre; Ple, Patrick; Stokes, Elaine Sophie Elizabeth; Mckerrecher, Darren
PATENT ASSIGNEE(S): Astrazeneca UK Limited, UK; Zeneca-Pharma S.A.
SOURCE: PCT Int. Appl., 346 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000047212	A1	20000817	WO 2000-GB373	20000208 <--
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
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EP 1553097	A1	20050713	EP 2005-4285	20000208
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IE, SI, LT, LV, FI, RO, MK, CY, AL

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PRIORITY APPLN. INFO.:	EP 1999-400305	A	19990210
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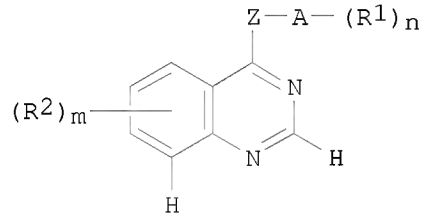
	WO 2000-GB373	W	20000208
	KR 2001-710133	A3	20010810
	US 2002-913020	A3	20020506

OTHER SOURCE(S): MARPAT 133:177183

GI



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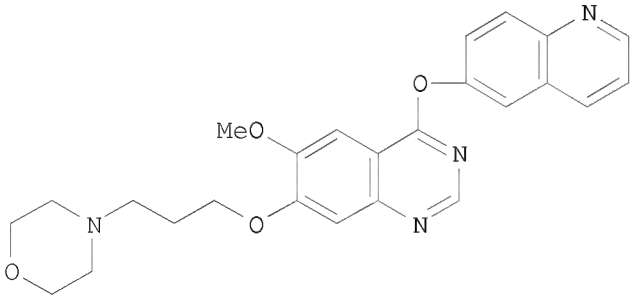


II

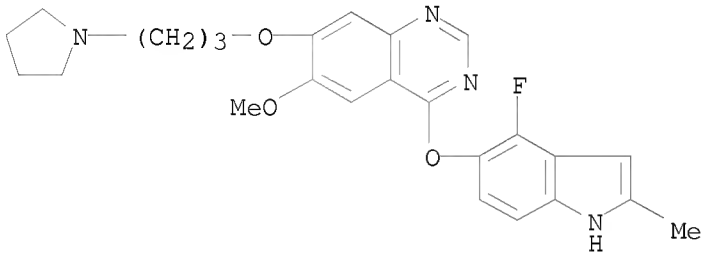
AB The title compds. (I) [wherein A = an 8-, 9-, 10-, 12- or 13-membered bicyclic or tricyclic ring optionally containing 1-3 O, N, and/or S heteroatoms; Z = O, NH, S, CH2, or a bond; n = 0-5; m = 0-3; R2 = H, OH, halo, CN, NO2, CF3, alkyl(sulfanyl), alkoxy, NR3N4, or R5X1; R3 and R4 = independently H or alkyl; X1 = a bond, O, CH2, OC(O), CO, S, SO, SO2, NR6CO, CONR7, SO2R8, NR9SO2, or NR10; R5 = H or (un)substituted alkyl,

alkenyl, alkynyl, or heterocyclyl, etc.; R6-R10 = independently H or (alkoxy)alkyl] were prepared for use in the production of an antiangiogenic and/or vascular permeability reducing effect in warm-blooded animals. For instance, II was synthesized in a 9-step sequence starting with the cyclization of 2-amino-4-benzyloxy-5-methoxybenzamide using Gold's reagent in dioxane to form 7-benzyloxy-6-methoxy-3,4-dihydroquinazolin-4-one (84%). I and the pharmaceutically acceptable salts thereof inhibit the effects of VEGF, a property of value in the treatment of a number of disease states including cancer and rheumatoid arthritis (no data).

IT 288383-20-0P, 4-(4-Fluoro-2-methylindol-5-yloxy)-6-methoxy-7-[3-(pyrrolidin-1-yl)propoxy]quinazoline
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(angiogenesis inhibitor; preparation of quinazolines as angiogenesis inhibitors by cyclization of 2-aminobenzamides and subsequent derivatization)

RN 288383-20-0 CAPLUS

CN Quinazoline, 4-[(4-fluoro-2-methyl-1H-indol-5-yl)oxy]-6-methoxy-7-[3-(1-pyrrolidinyl)propoxy]- (CA INDEX NAME)



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT